REMARKS

Claims 23 to 27, 30 to 34 and 44 to 55 were pending in the present application. In order to advance the prosecution of this case, claims 23 to 27 and 44 to 49 have been canceled without prejudice. Applicants reserve their rights to pursue these canceled claims in a continuing application. Claim 30 has been amended. The amendment corrects two typographical errors in the claim. Namely, an extra punctuation mark has been removed and the article "the" was replaced with "a" to put the claim in proper antecedent form. Additionally, the claim has been modified to indicate that the term "measuring base composition" is used to mean that the resultant base compositions identify the number of each residue in the amplification product. Support for this amendment is found throughout the specification, including the graphs and probability clouds illustrated in figures 17 and 18; the table illustrated in figure 25; and tables 4 to 7 in the specification. Accordingly, the amendments are fully supported by the specification and add no new matter. Applicants respectfully request entry of these amendments.

I. Claim Interpretation.

The office action states that the term "measuring base composition" is being broadly interpreted to include a variety of aspects of base composition. Applicants respectfully note that in claim 30, and claims dependent thereon, the step of measuring base composition includes identification of the number of each residue in the amplicon, independent of the linear arrangement of said residues. Such a measurement is found throughout the specification.

II. Response to Claim Rejections

35 USC § 112

Claim 27 has been rejected for failing to comply with the written description requirement. In order to advance the prosecution of the current case, claim 27 has been canceled. Thus, this rejection is rendered moot.

35 USC § 103(a)

1. **Jurinke et al Genetic Analysis: Biomolecular Engineering, 13 (1996) 67-71**

in light of Norder et al. J. Med. Virol. 31:215-221 (1990).

Claims 23 to 26, 30 to 34, 45 to 48 and 51 to 54 have been rejected as being obvious over Jurinke *et al* in light of Norder *et al.* Claims 23 to 26 and 45 to 48 have been canceled. Claim 30 has been amended. Jurinke is relied on for allegedly teaching the determination of viral bioagent characterizing information wherein Jurinke determines the presence or absence of HBV in a sample. Norder is relied on for teaching identification of different HBV subtypes using PCR amplification. Jurinke, Norder or the combination thereof do not teach or suggest measuring base composition of the amplification products. The references further fail to teach or suggest priming genes at regions that are conserved amongst members of a viral family and that flank regions that vary amongst the family to generate family member identifying amplicons. Although Applicants believe that the rejection is improper, in order to advance prosecution of this case, Applicants hereby incorporate the enclosed declaration under 37 C.F.R. 1.132 by Dr. Steven Buchsbaum. In his declaration, Dr. Buchsbaum notes that there was neither motivation, suggestion or teaching in the prior art for combining broad range priming with molecular mass measurements, and further notes the unexpected success of the technology. It is respectfully requested that the Examiner remove this rejection.

2. Jurinke et al Genetic Analysis: Biomolecular Engineering, 13 (1996) 67-71 in view of Norder et al. J. Med. Virol. 31:215-221 (1990) and in further view of Koster (WO 98/20166).

Claims 23 to 26, 30 to 34, 44 to 48 and 50 to 54 have been rejected as allegedly being obvious over Jurinke *et al* in light of Norder *et al.* and in further view of Koster. Claims 23 to 26 and 44 to 48 have been canceled. Claim 30 has been amended. Jurinke and Norder are relied as above. Koster is relied on for teaching respiratory viruses with known target sequences and for teaching base composition analysis of these known sequences. As stated above, Jurinke and Norder do not teach all of the elements of the claims. Koster does not make up for this defect. Koster's process uses known sequence and mutation sites (page 75 lines 12-13). New mutation sites are detected using digestion and hybridization capture techniques (lines 12-20). The current claims do not require that the sequence is known. Detection of new mutations do not require enzyme digestion or hybridization capture. Thus Jurinke, Norder, Koster or the combination thereof do not teach or suggest all of the elements of the claim. Although Applicants believe that the rejection is improper, in order to advance

prosecution of this case, Applicants hereby incorporate the enclosed declaration under 37 C.F.R. 1.132 by Dr. Steven Buchsbaum. In his declaration, Dr. Buchsbaum notes that there was neither motivation, suggestion or teaching in the prior art for combining broad range priming with molecular mass measurements, and further notes the unexpected success of the technology. It is respectfully requested that the Examiner remove this rejection.

3. Jurinke et al Genetic Analysis: Biomolecular Engineering, 13 (1996) 67-71 in view of Norder et al. J. Med. Virol. 31:215-221 (1990) and in further view of Fuerstanau *et al.* Rapid Communications In Mass Spectrometry (1995) 9:1528-1538.

Claim 27 has been rejected as being obvious over Jurinke *et al* in light of Norder *et al.* and in further view of Fuerstanau *et al.* Claim 27 has been canceled, thus, rendering the current rejection moot.

4. Jurinke et al Genetic Analysis: Biomolecular Engineering, 13 (1996) 67-71 in view of Norder et al. J. Med. Virol. 31:215-221 (1990) and in further view of Vanderhallen *et al.* J. Clin. Microbiol. (1998) 36(12):3463-3467.

Claims 49 and 55 have been rejected as being obvious over Jurinke *et al* in light of Norder *et al.* and in further view of Vanderhallen *et al.* Claim 49 has been canceled. Claim 55 depend from claim 30, which has been amended, and thus includes all the limitations thereof. Jurinke and Norder are relied as above. Vanderhallen is relied on for teaching analysis of a polymerase gene for EMCV typing using double RT-PCR and ABI sequencing. As stated above, Jurinke, Norder or the combination thereof do not teach or suggest all of the elements of the claim. Vanderhallen does not remedy this defect. Thus, the references do not render the claim obvious. Although Applicants believe that the rejection is improper, in order to advance prosecution of this case, Applicants hereby incorporate the enclosed declaration under 37 C.F.R. 1.132 by Dr. Steven Buchsbaum. In his declaration, Dr. Buchsbaum notes that there was neither motivation, suggestion or teaching in the prior art for combining broad range priming with molecular mass measurements, and further notes the unexpected success of the technology. It is respectfully requested that the Examiner remove this rejection.

Conclusions

In view of the foregoing, Applicants submit that the claims of the instant application

are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there should be any questions with regard to the claimed invention.

Respectfully submitted,

Jeff Landes, Esq.
Reg. No. 55,355
Direct 760-603-2528

Date: October 6, 2006

ISIS Pharmaceuticals, Inc.
1896 Rutherford Rd.
Carlsbad, CA 92008
Telephone: (760) 931-9200
Facsimile: (760) 603-3820